showed no difference in their degree of harm aversion for self versus other. By contrast, levodopa administration selectively reduced hyperaltruism, such that the typical pattern of increased harm aversion for others compared to self was abolished. Considering the known role of monoamines in motor function and response inhibition, it might be tempting to attribute this effect to shifts in response vigor or inhibitory control. However, the clever inclusion of action versus inaction trials (as noted above) permitted the authors to definitively rule out this alternative explanation.

These findings show that monoaminergic transmission influences prosocial and antisocial behavior by modulating how we represent and integrate value representations of outcomes for ourselves and others. Of course, no single study can do everything, and the systems-level mechanisms underlying these results remain unclear. Future pharmaco-fMRI and PET studies in humans could further illuminate the large-scale circuits and specific signal transduction pathways through which monoamines act to influence valuation during social decision-making. More work is needed to confirm the intriguing possibility, raised here and elsewhere [12], that social behavior is motivated by the same fundamental, domain-general mechanisms for value-learning and updating that drive non-social decision-making. It will be particularly important to explore how interactions between explicitly 'social' aspects of cognition (such as theory of mind and empathic resonance) and domain general valuation processes influence the mirrored representation of harm costs outside of self. That said, this work offers a strong rebuttal to inhibition-based 'brakes' accounts of social decision-making, and sheds important new light on the manner by which serotonergic and dopaminergic signaling shape social behavior.

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Chromosome Segregation: A Spatial Code to Correct Kinetochore–Microtubule Attachments

Julie K. Monda[1,2] and Iain M. Cheeseman[1,2,*]
[1]Whitehead Institute for Biomedical Research, Cambridge, MA, USA
[2]Department of Biology, MIT, Nine Cambridge Center, Cambridge, MA 02142, USA
*Correspondence: icheese@wi.mit.edu
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Erroneous kinetochore–microtubule interactions must be detected and corrected before a cell enters anaphase to prevent chromosome mis-segregation. Two new studies describe an Aurora A-mediated error correction mechanism based on the spatial position of a chromosome within the mitotic spindle.

Faithful segregation of the chromosomes to each daughter cell is an essential feature of cell division. Failure to accurately distribute the genomic material can result in aneuploidy and can have catastrophic consequences for the viability of a cell or organism. To segregate the chromosomes, microtubules emanating from the spindle poles must attach to the DNA through the kinetochore, a large, multi-protein complex assembled at the centromere of each chromosome. Proper segregation relies on the attachment of each replicated sister chromatid (or, in meiosis I, each homologous chromosome)

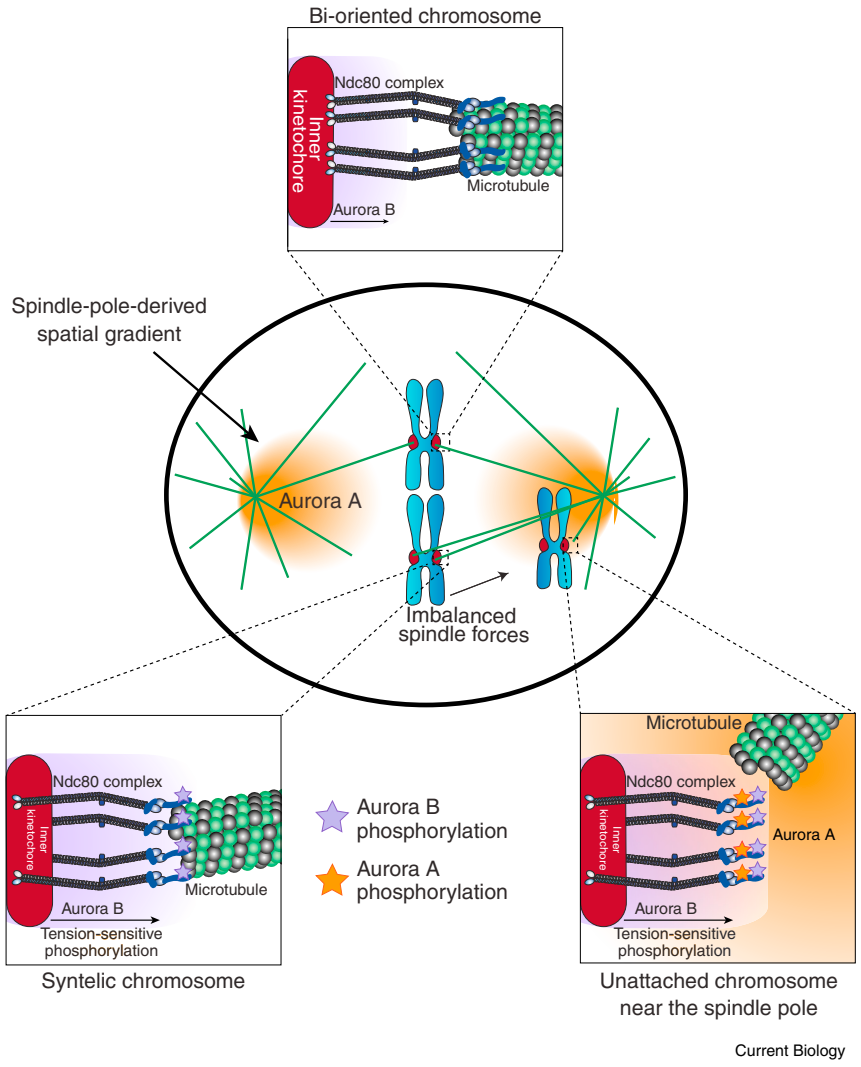

Figure 1. Error correction mechanisms for improper kinetochore–microtubule attachments.
Two mechanisms correct erroneous microtubule attachments. Because syntelic chromosomes are not under tension, Aurora B can phosphorylate outer kinetochore substrates, such as the Ndc80 complex (bottom left inset). The syntelic attachment also creates imbalanced spindle forces on the chromosome, pulling the chromosome towards the spindle pole to which it is attached. At the spindle pole, the outer kinetochore can be phosphorylated by Aurora A, in addition to Aurora B, destabilizing the microtubule attachment (bottom right inset). Bi-orientation of the chromosome results in balanced spindle forces and stretched kinetochores, thus preventing both Aurora A and Aurora B activity (top inset).

to microtubules from opposite spindle poles in a process termed bi-orientation. The cell must therefore be able to not only identify unattached kinetochores, but also distinguish bi-oriented from aberrantly attached kinetochores.

A key challenge lies in detecting erroneous attachments that may be superficially similar to those of bi-oriented chromosomes. For example, sister kinetochores may attach to microtubules emanating from the same spindle pole (syntelic attachment), instead of opposing spindle poles. In this case, one important difference is that the syntelically attached chromosome lacks the opposing spindle forces required to generate tension across the sister kinetochore pair. Previous work has demonstrated that this tension can be detected by Aurora B kinase [1]. Aurora B localizes to the inner centromere and, under low-tension conditions, phosphorylates kinetochore substrates such as Ndc80, the core microtubule-binding complex of the outer kinetochore [2]. Once a chromosome achieves bi-orientation, the kinetochores are stretched in opposing directions, moving the outer kinetochore substrates of Aurora B away from the inner centromere, thereby preventing their phosphorylation and stabilizing the proper attachment (Figure 1).

In addition to differences in tension at kinetochores, the spatial organization of the chromosomes could also help distinguish whether proper microtubule attachments have been formed. Bi-oriented chromosomes align at the metaphase plate in the middle of the cell through the balance of spindle forces from opposing poles. In contrast, improperly attached chromosomes experience uneven spindle forces, and are frequently situated closer to one spindle pole. In fact, an initial event in the correction of syntelic attachments is the movement of the improperly attached chromosome towards the spindle pole [3]. Mis-alignment of the chromosome within the spindle could provide an important signal to distinguish these improper attachments. Now, new work by Chmátal and Yang *et al.* [4] from the Lampson lab, and Ye *et al.* [5] from the Maresca lab in this issue of *Current Biology*, identifies a spatial mechanism for error correction in which another kinase of the Aurora family, Aurora A, destabilizes microtubule attachments from chromosomes in the vicinity of the spindle poles (Figure 1).

While the importance of Aurora B kinase in error correction is well established [6], the work from Ye *et al.* [5] and Chmátal and Yang *et al.* [4] now implicates Aurora A in error correction. The Aurora A and Aurora B kinases are found in most eukaryotes and share both high sequence identity as well as identical consensus phosphorylation sequences. In fact, several substrates have been reported to be phosphorylated by both Aurora A and Aurora B [7]. However, these phosphorylation events occur at different times in mitosis [7], and Aurora A and Aurora B display non-overlapping subcellular localizations. Specifically, unlike Aurora B, Aurora A localizes to the centrosome where it plays a key role in promoting centrosome maturation and spindle pole separation [8]. Thus, it has previously been thought that these two kinases perform distinct functions, primarily guided by their localization within the cell. However, because erroneously attached chromosomes are frequently located near a spindle pole,

both Chmátal and Yang *et al.* [4] and Ye *et al.* [5] hypothesized that, analogous to the role Aurora B plays at the inner centromere, Aurora A kinase may mediate error correction at the spindle pole.

To test this hypothesis, these studies exploited several elegant methods to generate increased frequencies of mis-positioned chromosomes. For example, Ye *et al.* [5] artificially increased the number of mis-positioned chromosomes by overexpressing the kinesin NOD. Previous work demonstrated that NOD overexpression leads to increased polar ejection forces that stabilize syntelic kinetochore–microtubule attachments [9]. Chmátal and Yang *et al.* [4] used a different approach, largely performing their experiments in mouse oocytes in meiosis I with asymmetric homologous chromosomes that are able to form microtubule attachments with both poles, but do not align on the metaphase plate. In this system, the homolog closest to a spindle pole is typically detached from microtubules, supporting the idea that spatial positioning of the chromosome plays a role in regulating kinetochore–microtubule attachments. Using these different experimental designs, both Ye *et al.* and Chmátal and Yang *et al.* demonstrated that overexpression of wild-type Aurora A reduced the number of kinetochore–microtubule attachments seen near the spindle poles. Similarly, disrupting Aurora A kinase activity using small molecule inhibitors, RNAi, or overexpression of a kinase-dead Aurora A mutant led to an increased frequency of microtubule attachments to kinetochores near the spindle pole.

To determine the timing in which the kinetochore–microtubule attachment was destabilized relative to the movement of the chromosome towards the spindle pole, Chmátal and Yang *et al.* [4] monitored the levels of the spindle assembly checkpoint protein Mad1 at kinetochores. Because Mad1 only localizes to unattached kinetochores, its levels provide a readout for the attachment status of an individual kinetochore [10]. Their data indicate that the movement of the chromosome towards the pole precedes Mad1 accumulation, nicely demonstrating that positioning of the chromosome near the spindle pole is the cause, not the consequence, of the destabilization of the kinetochore–microtubule attachment.

To investigate the mechanism by which Aurora A leads to destabilization of syntelic attachments near the spindle poles, Ye *et al.* [5] tested whether kinetochore substrates are phosphorylated by Aurora A. Using a kinetochore-targeted FRET sensor that is sensitive to phosphorylation by Aurora family kinases [11], the authors found an increase in phosphorylation of kinetochores near the spindle poles as compared with kinetochores of aligned chromosomes. Depletion of Aurora A by RNAi significantly reduced this phosphorylation of the FRET sensor near the spindle poles. Because the Ndc80 complex is a well characterized substrate of Aurora B in the tension-sensitive error correction system, Ye *et al.* [5] tested whether this complex may be an Aurora A substrate as well. The authors used a phospho-specific antibody to serine 55 of the Ndc80 complex subunit Hec1, a known site of Aurora B-mediated regulation [12–14]. Indeed, after treatment with an Aurora A inhibitor, they saw a decrease in phosphorylation of this site (Figure 1). This new work now reveals that Aurora A and Aurora B share a common substrate for the correction of improper microtubule attachments.

Although Aurora A and Aurora B were previously thought to perform unique functions, the work from Chmátal and Yang *et al.* [4] and Ye *et al.* [5] reveals that both kinases destabilize erroneous microtubule attachments. Interestingly, these kinases execute this function using at least one shared downstream target, the Ndc80 complex. However, because of the distinct subcellular localizations of Aurora A and Aurora B, these two related kinases utilize different mechanisms to identify inappropriate microtubule attachments. Together, the work from Chmátal and Yang *et al.* [4] and Ye *et al.* [5] convincingly identifies the presence of an Aurora A-mediated error correction mechanism based on the destabilization of microtubule attachments near the spindle poles.

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